60 Ceftazidime shows concentration-dependent killing on β-lactamase-overproducing biofilm of *Pseudomonas aeruginosa*

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Background: Resistance to ceftazidime due to hyper-production of chromosomally encoded β-lactamase is frequently encountered in *P. aeruginosa* isolates from patients with cystic fibrosis and chronic lung infections.
Aims: The purpose of this study was to investigate the role of β-lactamase in the pharmacokinetics and pharmacodynamics of ceftazidime on *P. aeruginosa* biofilms.
Methods: *Pseudomonas aeruginosa* PAO1 (7.8U, Nitrocefin hydrolysed/min /mg protein) and its overproducing β-lactamase mutant PAΔDDh2Dh3 (10933.7U) were used in this study. Biofilms of these two strains in flow-cells, microtiter-plate, and alginate beads were treated with different concentrations of ceftazidime (0.125 to 1024 μg/ml) and the killing effect was investigated. Colistin was used as a control antibiotic which effect is not affected by β-lactamase.
Results: Time-dependent killing of ceftazidime was observed in the *P. aeruginosa* PAO1 biofilms, but concentration-dependent killing activity was observed for β-lactamase-overproducing biofilms of *P. aeruginosa* in all the three models *in vitro*. Colistin showed concentration-dependent killing on both PAO1 and PAΔDDh2Dh3 biofilms.
Conclusions: The PK/PD indices of AUC/MBIC and C_{max} /MBIC (AUC, area under curve; C_{max}, maximum concentration; MBIC, minimal biofilm inhibitory concentration) are probably best to describe the effect of ceftazidime in β-lactamase-overproducing biofilms *P. aeruginosa*. This is probably due to the special distribution and accumulation of β-lactamase in the biofilm matrix which can hydrolyze the β-lactam antibiotics. The study will probably be useful to optimize the dosage regimens of β-lactam antibiotics for CF patients.

61 Colistin efficacy for children with cystic fibrosis (CF) at the first isolation of *Pseudomonas aeruginosa* (PA)

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Objective: To estimate efficiency of Colistin for children with CF with the first isolation of PA in different age groups.
Material: 30 patients with first isolation of PA aged from 0.2 to 15.8 years, the average age of patients was 5.4 (±4.9) years. A group of 19 children from 0 to 6 years (2.2±1.6), 2 groups of 11 children from 6 to 16 years (10.8±3.9). Colistin was administered at the dose of 0.5–2 million twice a day in addition to standard therapy of CF and oral ciprofloxacin 30 mg/kg/day during 21 days. Criterion of efficiency: microbiological of the sputum, spirometry (FEV_1, FVC in the second group), nutritional status.
Conclusions: The eradication of PA 1 group – 11%, 2 group – 18%, increase in FEV_1-7.4% ($p = 0.001$), FVC 5.5% ($p = 0.004$). Increase in BMI in the 1 group – 0.7% ($p = 0.001$), in the 2 – 0.4% ($p = 0.001$). Colistin is effective for eradication of PA in all age groups and is recommended for children with first isolate.

62 The use of trimethoprim suspension for anti-staphylococcal prophylaxis (ASP) in children with cystic fibrosis; the importance of a palatable preparation

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Background: Maintaining long-term antibiotic treatment in children who cannot take capsules requires a palatable suspension. When cefradine (velosef™) was taken off the market, we examined alternative preparations. We were keen not to use cefalexin due to adverse trial data suggesting increased *Pseudomonas* infection. With floxapen™ unavailable, we found flucloxacillin preparations unacceptable. We opted for trimethoprim suspension (commonly used in paediatrics for long-term therapy, with a unique spectrum of action).
Methods: We assessed the acceptability of trimethoprim suspension following the changeover (autumn 2010). We also assessed microbiology in children on trimethoprim, compared to an equivalent time period before the change.
Results: 27 children under the age of 6 were included. 6 children were commenced on capsules and did not require trimethoprim. Whilst on trimethoprim: 1 child did not tolerate it; 1 child had repeated *Staphylococcus aureus* (SA) growths; and 1 child grew MRSA several times. 1 child was switched to capsules after a short period. In the remaining 16 children, there were no growths of SA following the change to trimethoprim and less overall bacterial growth compared to the same time period before the switch.
Discussion: Overall trimethoprim suspension was well tolerated. Repeated SA and MRSA growths in 2 patients are a concern. There is no defined CF dose for trimethoprim; we used the standard dose in the BNF for children. Long term ASP is a challenge and palatable suspensions are essential in young children. These data suggest trimethoprim may offer an option in this age group but larger studies are required.

63 Time to recurrence and antimicrobial susceptibility of first-time detected *Achromobacter xylosoxidans* in respiratory tract specimens from patients with cystic fibrosis

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Objectives: Recent reports point to *Achromobacter xylosoxidans* as an emerging pathogen in cystic fibrosis (CF). While antimicrobial therapy has been shown to postpone the establishment of chronic infection for other bacteria, this needs to be explored for *A. xylosoxidans*.
Methods: Excluding documented cross-infections with an epidemic strain of Achromobacter, thirty-eight patients experienced a first-time detection of *A. xylosoxidans* at the two Danish CF centres during 2000–11. Using a Kaplan Meier estimation, the median time to recurrence was 7.5 months.
Results: Thirty-two first-time isolates of *A. xylosoxidans* were preserved, and the minimal inhibitory concentration (MIC) of 14 antibiotics was determined by Etest®. According to EUCAST guidelines, 94% of the isolates were susceptible to piperacillin-tazobactam (MIC_{90} = 6 mg/L), 88% to meropenem (MIC_{90} = 2 mg/L), 73% to colistin (MIC_{90} = 8 mg/L), 23% to ceftazidime (MIC_{90} = 24 mg/L), and 9% to tobramycin (MIC_{90} = 96 mg/L). MIC_{90} for trimethoprim-sulfamethoxazole was 0.047 mg/L, however interpretative criteria have not been established.
Nineteen patients received intravenous treatment with piperacillin-tazobactam or meropenem, or oral treatment with trimethoprim-sulfamethoxazole, for at least 14 days after the first isolation of *A. xylosoxidans*, and these patients had a median time to recurrence of 13.5 months. For the nineteen patients who did not receive any of these regimens, the median time to recurrence was 4.5 months.
Conclusion: Antibiotic treatment of primary *A. xylosoxidans* colonisation may postpone time to recurrence and establishment of chronic infection in cystic fibrosis.